

R E M A R K S

Status of the Claims

Claims 1, 2, 5-30, 32, 34-38 and 40-41 are pending in this application. Claims 33 and 39 have been canceled. Claims 40 and 41 have been added. No claims have been amended. Support for new claims 40 and 41 is found in the specification at page 10, lines 21-25. No new matter has been added by the above claim amendments.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claim 39 as indefinite. Applicant cancels claim 39. As such, the rejection is moot and should be withdrawn.

However, Applicant submits the following arguments in connection with new claims 40 and 41. Applicant submits that the new claims 40 and 41 particularly and distinctly recite the subject matter of the invention and do not recite "mutated". After the compounds are synthesized and separated, the compounds are then screened for their ability to act as substrates for the catalyst or modulators of catalytic activity. Therefore, the compounds interact with the catalysts in a biochemical method.

**Rejections under 35 U.S.C. § 103(a)**

The Examiner rejects claims 1, 2, 5-12, 15-30 and 32-36 as obvious over Mehta et al. U.S. Patent 6,306,590 (Mehta '590) in view of Frank, *Spot Synthesis*. Applicant traverses the rejection and respectfully requests the withdrawal thereof.

The present invention is directed to a method for the sequential synthesis, separation and direct screening of compounds in the same bulk of a stationary phase. The method offers a large degree of flexibility, most importantly with respect to the number of reactions, which can be performed in the same bulk of a stationary phase, but also with respect to techniques used for separation of the products.

Mehta '590 generally discloses a "multiphasic microfluidic apparatus" where synthesis and separation of the components occur in separate, albeit communicating compartments. The components are typically made or purified in the first phase and separated in the second phase. With respect to products generated in a PCR reaction, the apparatus of Mehta '590 provides the possibility of performing synthesis, separation and screening in a sieving matrix. Mehta '590 fails to disclose a screening step where screening of the separated products is by biological or biochemical methods.

Frank describes a method for performing simultaneous parallel

synthesis of compounds at distinct areas on the same sheet of support matrix and subsequently screening these compounds. The publication teaches how multiple reactions can be performed on the same sheet of support matrix by arraying narrowly spaced synthesis spots in two dimensions. Frank discloses screening by biological or biochemical methods of product resulting from a multiplicity of reactions on a stationary phase.

Applicant submits that one of ordinary skill in the art would not be motivated to combine the cited references to arrive at the present invention because the primary reference does not disclose or suggest all the limitations of the present invention and the secondary reference teaches away from the present invention. Thus, one of ordinary skill in the art would not be able to achieve the same results as the present invention.

In the present invention, it is possible to perform a "plurality of reactions in the same bulk of a stationary phase". Mehta '590 on the other hand does not provide such a "bulk". If a plurality of reactions is to be performed in the Mehta '590

apparatus, it must occur in a "multiplicity of multiphasic compartments", which cannot be one continuous bulk phase. In other words, it is possible to perform several reactions within the same apparatus, however each reaction will be physically separated from the others.

Yet, in the present invention, the reactions are performed on a bulk of a stationary phase as provided by the present invention and all individual reactions will be fluidically interconnected.

In the assay described in Frank, no separation step occurs on the same bulk. The mode of arraying narrowly spaced synthesis spots in two dimensions on the same support in Frank clearly precludes any kind of separation, such as by chromatography. Furthermore, in Frank the compounds must be anchored to the support by covalent binding, see e.g. page 9220, lines 16-18: "The paper sheet needs to be chemically derivatised to introduce suitable anchor functions for peptide synthesis at the spot positions. These anchors also serve as spacer arms to improve the accessibility of the immobilized peptides". It is also described how the individual spots are cut or punched out and transferred to separate tubes for assaying. As such, there is no possibility for separation of the products by chromatography or any other means in the same bulk phase.

Applicant submits that one of ordinary skill in the art would not be motivated to combine Mehta '590 with Frank to arrive at the present invention because Frank teaches away from have a separation step by immobilizing the resulting compounds and Mehta '590 fails to disclose or suggest having the same bulk of a stationary phase for all steps, but instead uses separate compartments. As such, Applicant submits that no *prima facie* case of obviousness has been established and the rejection should be withdrawn.

The Examiner also rejects claims 13 and 14 as obvious over Mehta '590 in view of Frank and further in view of Hudak USP 6,034,361 (Hudak '361). Applicant traverses the rejection and respectfully requests the withdrawal thereof.

Applicant submits that as claims 13 and 14 depend from claim 1, the arguments above regarding no motivation to combine Mehta '590 and Frank also apply to this rejection. In as much as Hudak '361 fails to compensate for the deficiencies in Mehta '590 and Frank, Applicant submits that the rejection should be withdrawn.

The Examiner also rejects claims 37 and 38 as obvious over Mehta '590 in view of Frank and further in view of Bastaillard USP 5,482,372 (Bastaillard '372) or Brocklehurst USP 5,739,003

(Brocklehurst '003). Applicant traverses the rejection and respectfully requests the withdrawal thereof.

Applicant submits that as claims 37 and 38 depend either directly or indirectly from claim 1, the arguments above regarding no motivation to combine Mehta '590 and Frank also apply to this rejection. In as much as Bastaillard '372 and Brocklehurst '003 fail to compensate for the deficiencies in Mehta '590 and Frank, Applicant submits that the rejection should be withdrawn.

The Examiner also rejects claim 39 as obvious over Mehta '590 in view of Frank and further in view of DE 3701833 (DE '833). Applicant traverses the rejection and respectfully requests the withdrawal thereof.

Applicant submits that as claim 39 depends indirectly from claim 1, the arguments above regarding no motivation to combine Mehta '590 and Frank also apply to this rejection. In as much as DE '833 fails to compensate for the deficiencies in Mehta '590 and Frank, Applicant submits that the rejection should be withdrawn.

**Objection to Drawings**

The Official Draftperson objects to the Figures filed May 10, 2002. Applicant submits herewith revised Figures 1-4 and

11-19 to remove copy machine marks. As such, the objection should be withdrawn.

**Conclusion**

As Applicant has addressed and overcome all rejections in the Office Action, Applicant respectfully requests that the rejections be withdrawn and that the claims be allowed.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant respectfully petitions for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of \$110.00 is attached hereto.

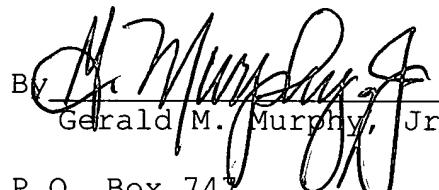
Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kecia Reynolds (Reg. No. 47,021) at the telephone number of the undersigned below.

**Attached hereto is a marked-up version of the changes made to the application by this Amendment.**

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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GMM/KJR:bmp  
0459-0490P

Attachment: Version with Markings to Show Changes Made

(Rev. 02/20/02)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 33 and 39 have been cancelled.

Claims 40 and 41 have been added.